

REMARKS

Claims 1-12 and 21-48 are pending in the application. Claims 13-20 were previously cancelled without prejudice or disclaimer. Applicants reserve the right to pursue the cancelled subject matter in one or more continuing applications.

Applicants acknowledge the Examiner's withdrawal of the following rejections: (i) rejection of claims 1-3 under §102(e) in view of Davidson et al. (US 2005/0106731); and (ii) rejection of claims 1-13 and 21-27 under 35 U.S.C. § 103(a) over Davidson et al. [US2005/0106731], Klug et al. [European J. of Physiology, 441(6 Suppl): R205 (2001)], Brown et al. [WO 94/19493], Siddique et al. [Neurology, 47 (Suppl 2): S27-S35 (1996)], and Kunst et al. [Nature Genetics, 15: 91-94 (1997)].

With respect to the newly applied rejections, Applicants respectfully request reconsideration and examination of this application and the timely allowance of the pending claims in view of the arguments presented below.

I. Request for Withdrawal of the Finality of the Office Action

It is respectfully submitted that the Final Rejection of the instant application may be premature. In particular, Applicants respectfully submit that the instant rejections (newly applied under 35 U.S.C. §103) may be improper since they rely *inter alia* on a reference (Kruetzer et al. [US 2005/0074757]) that does not have an effective prior art date prior to priority date of the instant application. Applicants' grounds are set forth below. Accordingly, Applicants respectfully request reconsideration and withdrawal of the finality of the Office Action. Applicants also respectfully request consideration of the enclosed Supplemental Information Disclosure Statement and the cited documents therein (including all of the translation documents that have been provided for the German priority documents of Kruetzer et al.).

II. Claim Rejections -35 U.S.C. §103

(a) Rejection of claims 1-12 and 28-40

The Examiner has newly rejected claims 1-12 and 28-40 under 35 U.S.C. §103(a) in view of Kreutzer et al. [US 2005/0074757], Elbashir et al. [The EMBO Journal, 20(23), 2001],

Klug et al. [European J. of Physiology, 441(6 Suppl): R205 (2001)], Brown et al. [WO 94/19493], Siddique et al. [Neurology, 47 (Suppl 2): S27-S35 (1996)], and Kunst et al. [Nature Genetics, 15: 91-94 (1996)]. In particular, the Examiner points to paragraphs [006], [0015], [0023] and [0060-0063] of Kreutzer et al. in support of the assertion that “Kruetzer et al. have taught to inhibit disease-associated mutants that contain point mutations such that the mutant is inhibited while the wild-type is not”(see page 3 of Final Office Action). Thus, the Examiner has relied on Kreutzer as a primary reference for the §103 rejection.

Applicants respectfully traverse.

Applicants respectfully submit that the §103(a) rejection is improper since it relies on a reference (Kruetzer et al., [US 2005/0074757]) that does not have an effective prior art date prior to Applicants’ priority date. To assist in reviewing Applicants’ argument, a schematic timeline of the priority, filing and publication dates of Kruetzer et al. is enclosed herewith as Appendix A.

Applicants note that Kruetzer et al. [US 2005/0074757] was published on April 7, 2005 and well after the filing date (November 4, 2003) of the instant application. Thus, since Kruetzer et al. is neither a §102(a) or §102(b) reference, it must be available as §102(e) prior art to be properly relied upon in a §103 rejection. Applicants respectfully submit that ***Kruetzer et al. is an improper §102(e) prior art reference*** for at least the following reasons:

- (1) *Kruetzer et al. [US 2005/0074757] is not available as §102(e) prior art as of its Actual Filing Date (March 7, 2003).*

Applicants note that Kruetzer et al. was filed on March 7, 2003. However, Applicants claim priority to US Provisional App. No. 60/423,507 filed November 4, 2002. Applicants are of the opinion that all of the pending claims are fully entitled to this earlier priority date and that Kruetzer et al. is not §102(e) prior art as of its filing date. Since the Examiner has not contested Applicants’ priority claim, Applicants assume that the Examiner shares the same opinion. If the Examiner has any reason to question Applicants’ priority claim, the Examiner is respectfully requested to state these reasons for the record.

- (2) *Kruetzer et al. [US 2005/0074757] is not available as §102(e) prior art as of its Foreign Priority Dates*

Applicants note that Kruetzer et al. [US 2005/0074757] claims priority to four (4) German priority documents: (a) DE 10155280.7, filed October 26, 2001; (b) DE 10158411.3, filed November 29, 2001; (c) DE 10160151.4, filed December 7, 2001; and (d) DE 10235620.3, filed August 2, 2002. As the Examiner is aware, a reference cannot be applied as §102(e) prior art based on a foreign priority application (see MPEP §706.02(f)(1)). Thus, none of German priority documents (a)-(d) can be relied upon to support the instant §102(e)/§103 rejection.

Notwithstanding the above, Applicants have provided English language translations of each of the German priority documents for the Examiner's consideration (see references B1-B4 in the attached IDS). With respect to priority documents (a), (b) and (d), Applicants are unaware of any patent publications that correspond to these documents. Furthermore, Applicants note that German priority document (c) (DE 10160151.4) appears to have published on June 26, 2003 (see reference B10 in attached IDS), a date that is well after Applicants earliest priority date (November 4, 2002). Accordingly, Applicants submit that German priority documents (a)-(d) are also disqualified as prior art under both §102(a) and §102(b).

- (3) *Kruetzer et al. [US 2005/0074757] is not available as §102(e) prior art as of its PCT Priority Dates*

Applicants note that Kruetzer et al. [US 2005/0074757] claims priority to three (3) PCT applications: (a) PCT/EP02/00152 (WO 02/055693), filed January 9, 2003; (b) PCT/EP02/00151 (WO02055692), filed January 9, 2002; and (c) PCT/EP02/11969, filed October 25, 2002. Under revised 35 U.S.C §102(e)(1), an international filing date which is on or after November 29, 2000 is a United States filing date if the international application designated the United States, was published by the World Intellectual Property Organization (WIPO) under the Patent Cooperation Treaty (PCT) Article 21(2) in *the English language* (emphasis added). Therefore, the prior art date of a reference under 35 U.S.C. §102(e) may

be the international filing date if the three conditions above are met. International applications, which: (1) were filed prior to November 29, 2000, or (2) did not designate the U.S., or (3) **were not published in English** under PCT Article 21(2) by WIPO, may not be used for prior art purposes under 35 U.S.C. 102(e). Applicants submit that although each of the 3 PCT applications were filed after November 29, 2000 and designated the US, **all of the documents were published in German** (see references B7-B9 in the attached IDS). Thus, the international filing dates of these documents cannot be relied upon in the instant §102(e)/§103 rejection.

Notwithstanding the above, Applicants are aware two English-language Canadian patent publications (CA2432350 and CA2432341, see references B5 and B6 in the attached IDS) which correspond to PCT/EP02/00152 and PCT/EP02/00151, respectively. Both of these Canadian publications appear to have published on July 18, 2002. Nevertheless, the passages of Kreutzer et al. relied upon by the Examiner (i.e., paragraphs 006, 0015, 0023, and 0060-0063) cannot be found in either Canadian publication.

With respect to the third German-language PCT (PCT/EP02/11969), filed October 25, 2002, Applicants have provided a translation of this document for the Examiner's consideration (see reference B9 in the attached IDS). Applicants are not aware of an English-language patent document that corresponds to this PCT. Without specifically addressing the disclosure of this PCT, Applicants submit that it does not serve as either §102(a), §102(b) or §102(e) prior art since it was published in German on May 1, 2003 and after Applicants' earliest priority date of November 4, 2002.

For at least the reasons given above, Applicants submit that Kreutzer et al. and its corresponding patent family members are unavailable as prior art references. Since the Examiner relies on Kreutzer et al. as a primary prior art reference for the instant §103 rejection, and since none of the secondary references (Elbashir et al., Klug et al., Brown et al., Siddique et al., or Kunst et al.), whether alone or combined, teach or suggest the claimed invention absent the primary reference, Applicants submit that the §103 rejection is obviated. Moreover, Applicants respectfully submit that combination of references cited by the Examiner not only fails to teach or suggest each and every element recited in the claims, but they fail to provide an enabling teaching of allele-specific RNA silencing. Finally, Applicants submit that the prior art

lacked any teaching, suggestion or motivation to combine the references. Thus, the combination of cited references fails to establish a *prima facie* evidence of obviousness. The same would be true even if the Examiner were to rely on one or more of the Kruetzer et al. priority documents in combination with any or all of the cited documents.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

(b) Rejection of claims 41-48

The Examiner has newly rejected claims 41-48 under 35 U.S.C. §103(a) in view of Kreutzer et al. [US 2005/0074757], Elbashir et al. [The EMBO Journal, 20(23), 2001], Klug et al. [European J. of Physiology, 441(6 Suppl): R205 (2001)], Brown et al. [WO 94/19493], Siddique et al. [Neurology, 47 (Suppl 2): S27-S35 (1996)], and Kunst et al. [Nature Genetics, 15: 91-94 (1996)] as applied to claims 1-12 and 28-40 above, and further in view of Brummelkamp et al. [Science Express, March 21, 2002]. Here again the Examiner has relied on Kreutzer et al. as a primary reference for the §103 rejection. Without again addressing the alleged teachings in the cited references, Applicants submit that the rejection is improper for at least the same reasons given above with respect to the rejection of claims 1-12 and 28-40. Accordingly, reconsideration and withdrawal of the rejection has been respectfully requested.

III. Claim Objections

Claim 5 has been objected to under 37 CFR 1.75(c) as being of improper dependent form. The Examiner correctly notes that Claim 5 requires that the siRNA is targeted to the gain of function mutation, but is of the opinion that “the context of the claims from which this claim depends requires that this limitation be met prior to its recitation in the subject claim”.

Applicants respectfully disagree and submit that the base claims only require that the siRNA specifically target the mutant allele. Accordingly, any mutations which differ from the wild-type allele, including gain-of-function mutations and other nucleotide mutations within the mutant allele, can be specifically targeted by the siRNA. Accordingly, Applicants respectfully submit that claim 5 does indeed further limit the claims from which it depends.

CONCLUSION

In view of the above amendment and response, Applicants believe the pending application is in condition for allowance. If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' attorney, Debra J. Milasincic, Esq., at (617) 227-7400.

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Respectfully submitted,

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